

In The Claims:

1. - 28. (Cancelled)

29. (Currently amended) An *in vivo* assay to identify molecular markers linked to phenotypic stability of a chondrocyte cell population comprising:

- a) injecting intramuscularly or subcutaneously in a non-human animal a suspension of isolated or expanded cells in an iso-osmotic liquid, the same suspension comprising articular chondrocytes in an amount equivalent to at least 1×10^6 chondrocytes as applied to immune-deficient mice,
- b) allowing the formation of cartilaginous tissue,
- c) sacrificing the animal,
- d) evaluate evaluating the formed cartilage histologically for stable, non-vascularised cartilage *in vivo*, and
- e) ~~identify~~ identifying positive or negative molecular markers of those isolated or expanded cells evaluated in step d) which form stable, non-vascularised cartilage *in vivo*.

30. (Previously presented) An assay to identify molecular markers according to claim 29, comprising using freshly isolated or serially passaged cells using differential gene expression analysis methods including differential display, subtractive hybridization, subtracted libraries or cDNA chips and cDNA arrays.

31. (Currently amended) A method to identify cells having chondrocyte phenotypic stability comprising determining the expression of BMP-2 and/or FGFR-3 and/or markers ~~co-detectable~~ co-detectable with these markers and/or specific reporter constructs associated with these markers.

32. (Previously presented) A method to identify cells having chondrocyte phenotypic stability according to claim 31 further comprising determining that activin-like kinase-1 (ALK-1) is not expressed, and/or markers co-detectable with these markers and/or specific reporter constructs associated with these markers are not expressed.
33. (Previously presented) A method to identify cells with chondrocyte phenotypic stability comprising hybridising to messenger RNA from cells, sets of DNA probes provided on DNA arrays or DNA chips.
34. (Previously presented) A method to identify phenotypically stable primary chondrocytes and chondrocytes, after at least one passage, that remained phenotypically stable comprising detecting sets of positive markers, said positive markers being selected from expressed BMP-2, FGFR-3, markers co-detectable with these markers or specific reporter constructs associated with these markers or markers determined by an in vivo assay according to claim 29.
35. (Previously presented) Method to monitor passage by passage cell expansion and/or to predict when cell expansion must be stopped and/or to recover cells that have already lost their phenotypic stability only when needed and/or to provide a means for quality control of cells to be used for autologous cell transplantation and/or selecting from a cell population only those cells that retain their chondrocyte phenotypic stability,

comprising detecting the expression of molecular markers of chondrocyte phenotypic stability selected from the group of:

- markers determined by the assay comprising: a) injecting intramuscularly or subcutaneously in a non-human animal a suspension of isolated or expanded cells in an iso-osmotic liquid, the same suspension comprising articular chondrocytes in an amount equivalent to at least 1×10^6 chondrocytes as applied to immune-deficient mice, b) allowing the formation of cartilaginous tissue, c) sacrificing the animal, d) evaluate the formed cartilage histologically for stable, non-vascularised cartilage in vivo, and e) identify positive or negative molecular markers of those isolated or expanded cells evaluated in step d) which form stable, non-vascularised cartilage in vivo,

- BMP-2 and/or FGFR-3 and/or markers co-detectable with these markers and/or specific reporter constructs associated with these markers,

- expressed activin-like kinase-1 (ALK-1) as a marker negatively associated with chondrocyte phenotypic stability, and/or markers co-detectable with these markers and/or specific reporter constructs associated with these markers.

36. (Previously presented) Method according to claim 35 comprising sorting cells via monoclonal or polyclonal antibodies against negative or positive markers or co detectable markers for the monitoring of cell expansion and/or predicting when cell expansion must be stopped and/or selecting cells which have lost chondrocyte phenotypic stability and/or selecting cells which retain chondrocyte phenotypic

stability.

37. (Cancelled)

38. (Cancelled)

39. (Previously presented) Cells selected according to claim 33, these cells having chondrocyte phenotypic stability.

40. (Previously presented) Cells selected according to claim 35, these cells having chondrocyte phenotypic stability.

41. (Previously presented) An *in vivo* assay

- to predict the outcome of autologous cell transplantation using the cells selected by the method of claim 33
- or to optimize cell culture conditions and manufacturing processes for a specific application in tissue engineering of cells selected by the method of claim 33,
- or to evaluate the possibility that for the cells selected by the method of claim 33, said selected cells being used for autologous cell transplantation or being used in a pharmaceutical composition, that a treatment administered to the selected cells can hamper or enhance the anchorage-independent growth of said population as well as its phenotypic stability;

the *in vivo* assay comprising: subcutaneous or intramuscular injection in a

non-human animal of a suspension of the selected cells in an iso-osmotic liquid, the same suspension comprising articular chondrocytes in an amount equivalent to at least 1×10^6 chondrocytes as applied to immune-deficient mice.

42. (Previously presented) An *in vivo* assay

to predict the outcome of autologous cell transplantation using the cells selected by the method of claim 35

or to optimize cell culture conditions and manufacturing processes for a specific application in tissue engineering of cells selected by the method of claim 35,

or to evaluate the possibility that for the cells selected by the method of claim 35, said selected cells being used for autologous cell transplantation or being used in a pharmaceutical composition, that a treatment administered to the selected cells can hamper or enhance the anchorage-independent growth of said population as well as its phenotypic stability;

the *in vivo* assay comprising: subcutaneous or intramuscular injection in a non-human animal of a suspension of the selected cells in an iso-osmotic liquid, the same suspension comprising articular chondrocytes in an amount equivalent to at least 1×10^6 chondrocytes as applied to immune-deficient mice.

43. (Previously presented) Transplanting cells to a connective tissue site in a patient or seeding with cells any prosthetic device intended to be anchored into a

mammal, said cells retaining their chondrocyte phenotypic stability and selected according to the method of claim 33.

44. (Previously presented) Transplanting cells to a connective tissue site in a patient or seeding with cells any prosthetic device intended to be anchored into a mammal, said cells retaining their chondrocyte phenotypic stability and selected according to the method of claim 35.

45. (Previously presented) A therapeutic composition for humans including cells selected according to claim 33, optionally further including at least a pharmaceutically acceptable carrier and/or a growth factor.

46. (Previously presented) A therapeutic composition for humans including cells selected according to claim 35, optionally further including at least a pharmaceutically acceptable carrier and/or a growth factor.

47. (Previously presented) A diagnostic comprising the DNA chips of claim 33.

48. (Cancelled)

49. (Previously presented) A cell culture exhibiting chondrocyte phenotypic stability. in which the cells express a ratio of

BMP-2 and/or FGFR-3 as molecular markers positively associated with chondrocyte phenotypic stability and/or markers co-detectable with these markers and/or specific reporter constructs associated with these markers to

activin-like kinase-1 (ALK-1) as a molecular marker negatively associated with chondrocyte phenotypic stability and/or markers co-detectable with this marker and/or specific reporter constructs associated with this negative marker, which is greater than 1, preferably greater than 2.

50. (Previously presented) A cell culture exhibiting chondrocyte phenotypic stability in which the cells do not express activin-like kinase-1 (ALK-1) and/or markers co-detectable with this marker and/or specific reporter constructs associated with these markers as molecular markers negatively associated with chondrocyte phenotypic stability.